ULTRASTRUCTURE OF LYSOSOME

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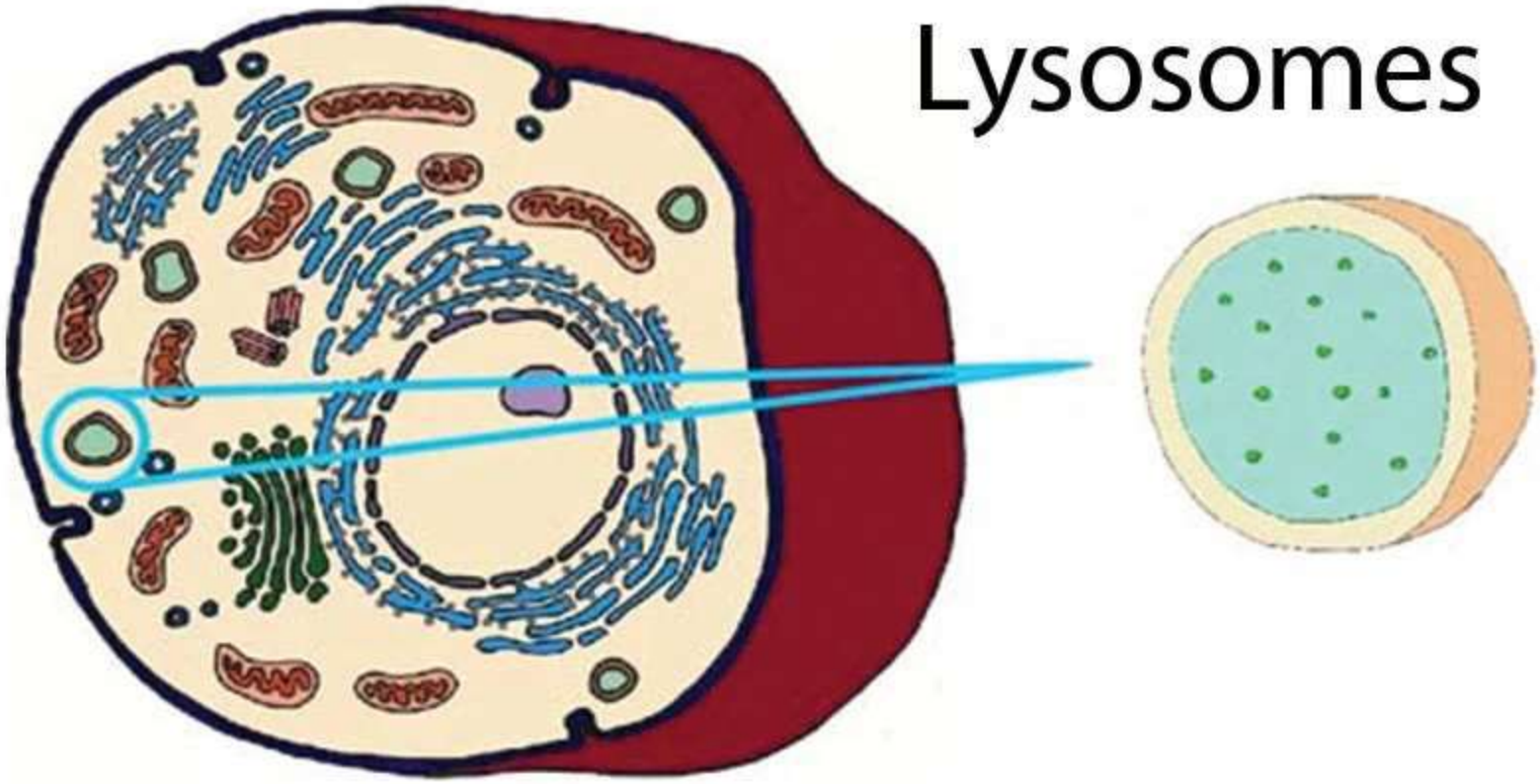
Introduction

- Lysosomes are discovered by Belgian biochemist Christian de Duve in 1955, later on it is reported by P. Matile in 1964 in Neurospora (a fungus).
- They are membranous vesicles appears as tiny bag like structures with an average diameter of 0.23 – 0.5µ.
- They are regarded as the “digestive system of the cell” or “suicidal bag “.
- The term lysosome is derived from latin word “Lyein” meaning to dissolve or loosen and “soma” meaning body.
- They are mostly present in animals cells while only in some lower plant groups (slime moulds and sprophytic fungi). Meristamatic tissue of higher plants also found to contain lysosomal vesicles.
- They are found in most abundant numbers in cells having secretory functions such as liver cells, pancreatic cells, kidney cells, spleen cells, leucocytes, macrophages, etc.
- They are originated from cisternae of Golgi body or from the tubules of endoplasmic reticulum.
- In animals, it is found suspended in cytoplasm in all cell types except RBCs.

Lysosome: A subcellular organelle



Structure of lysosome

- They have not a definite shape; they are pleomorphic.
- They are mostly globular or granular in appearance.
- They are of 0.2 – 0.5 μm in diameter and are surrounded by a single lipoprotein membrane unique in composition.
- The membrane are glycosylated proteins named as lysosomal associated membrane proteins (LAMP) and lysosomal integral membrane proteins (LMP).
- Both LAMPs (LAMP-1 & LAMP-2) and LIMPs (LIMP-1 & LIMP-2) are studded in the inner surface of the membrane forming a coat there.
- Inside the membrane, the organelle contains different hydrolytic enzymes in crystalline form (pro-enzyme).

Types of lysosomes

There are two types of lysosomes; primary lysosome and secondary lysosomes.

- Primary lysosome
  - Small sac-like structures, which contain enzymes synthesized by the rough endoplasmic reticulum.
  - It is actually a storage vesicles called as storage granules storing enzymes.

- Secondary lysosome
  - It is formed by the fusion of primary lysosome with endosome/phagosome.
  - It therefore contains engulfed particles in addition to the hydrolyzing enzymes.
  - Engulfed/endocytosed particles are progressively digested by the enzymes.

Types of lysosomes

There are three characteristic subcellular vesicles that are characterized as secondary lysosomes on the basis of morphological feature. These vesicles are following:

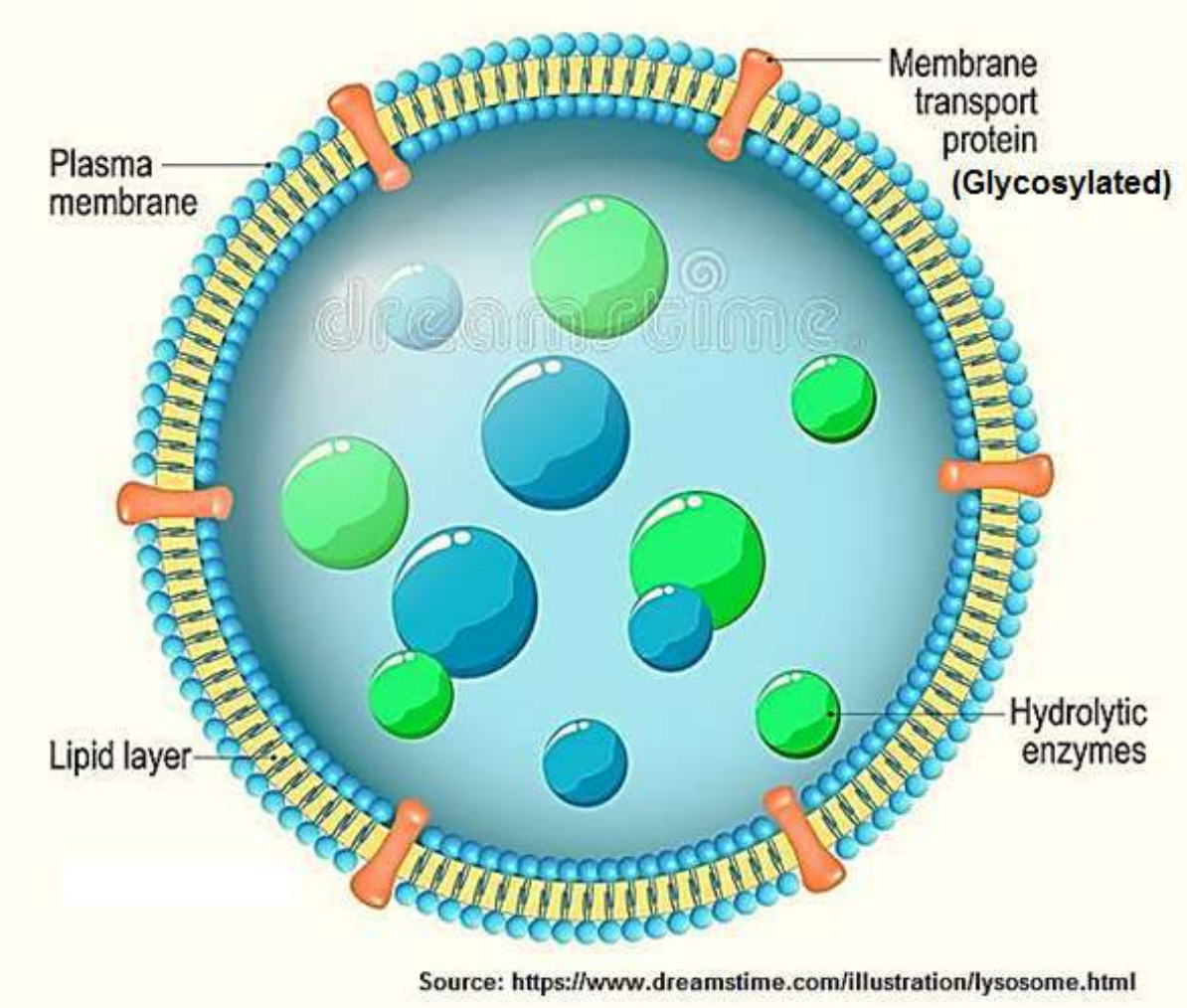
- Digestive vaculole
  - Small sac-like bodies containing foreign materials engulfed by the cell.
  - In this structure, digestion or breaking down of the foreign body takes place.

- Residual bodies
  - These are secondary body with unhydrolysed residues due to incomplete digestion of ingested particles.
  - The unhydrolysed particles or residues either remain inside the lysosome or discharged out.

- Autophagic vaculole
  - During autolysis (a process in which lysosomes release hydrolases in damaged or ageing cells to digest them), these vaculole is formed known as autophagosomes.

Suicidal bag of the cell

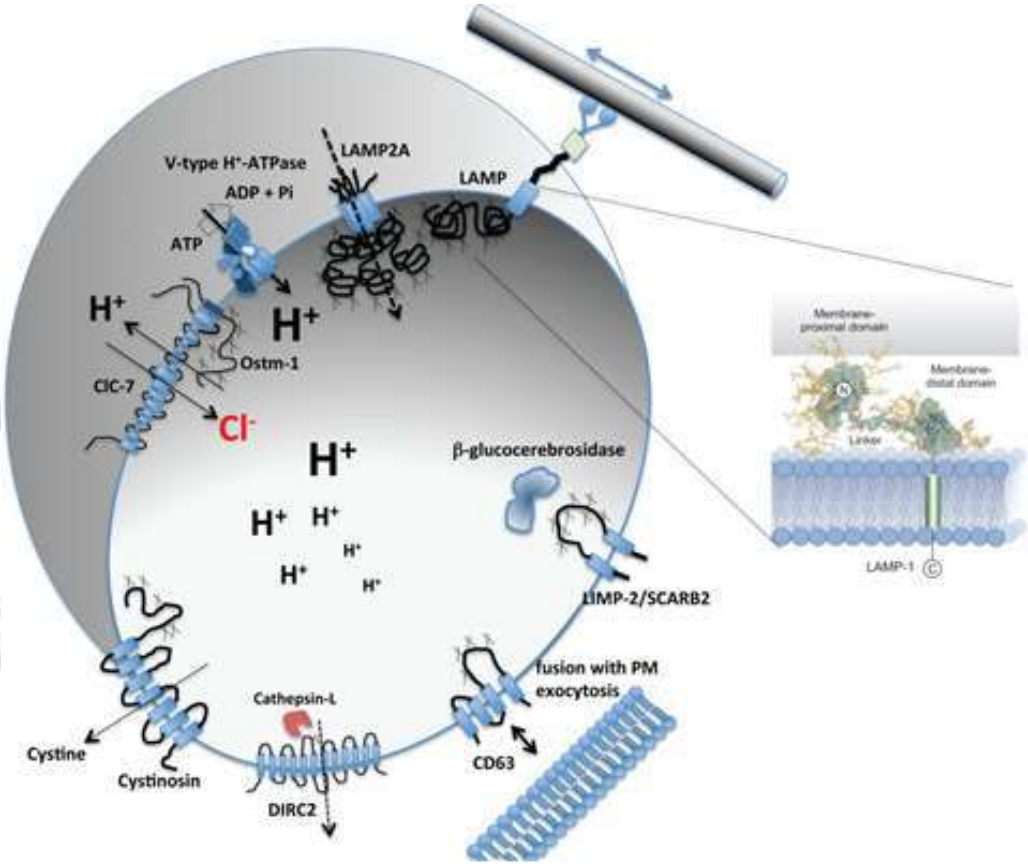
Structure of lysosome



- These proteins have essential role in lysosomal acidification (proton transport), transport of metabolites resulting from hydrolytic degradation, and interaction of and fusion with other membrane system.
- Glycoproteins LAMP-1 and LAMP-2 are essential for regulation of lysosomal motility and participating in control of membrane fusion events

Proton transport and activation of enzyme

- The lysosomes mainly have H^+-ATPase (also known as vacuolar ATPase, V-ATPase) which transports H^+ ion inside the lumen.
- Proton influx and fusion of endosome activate the lysosomal enzymes which are otherwise inactive.



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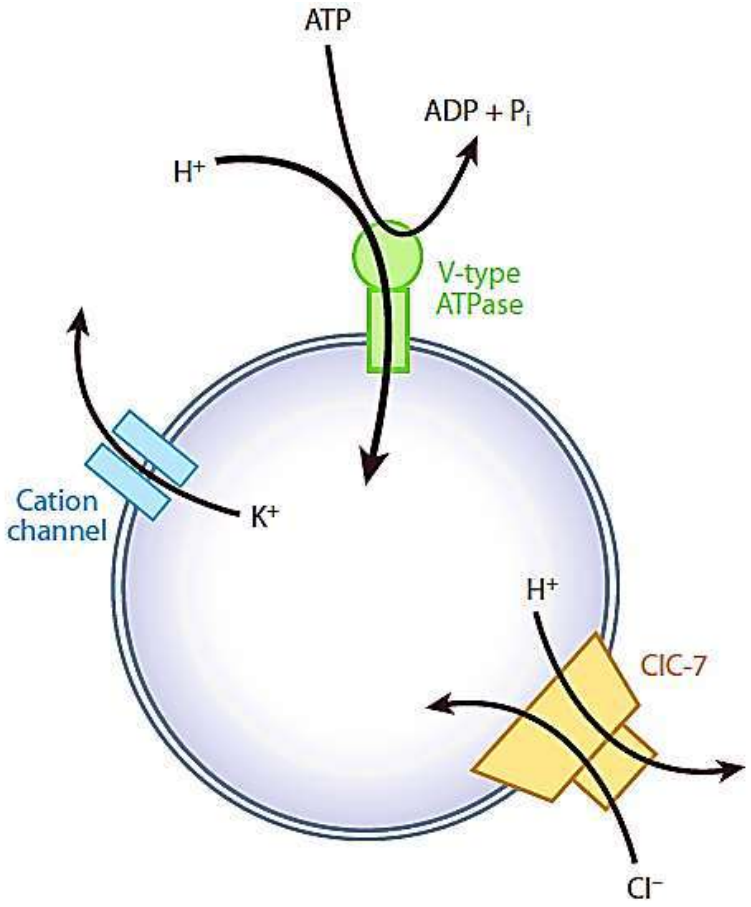
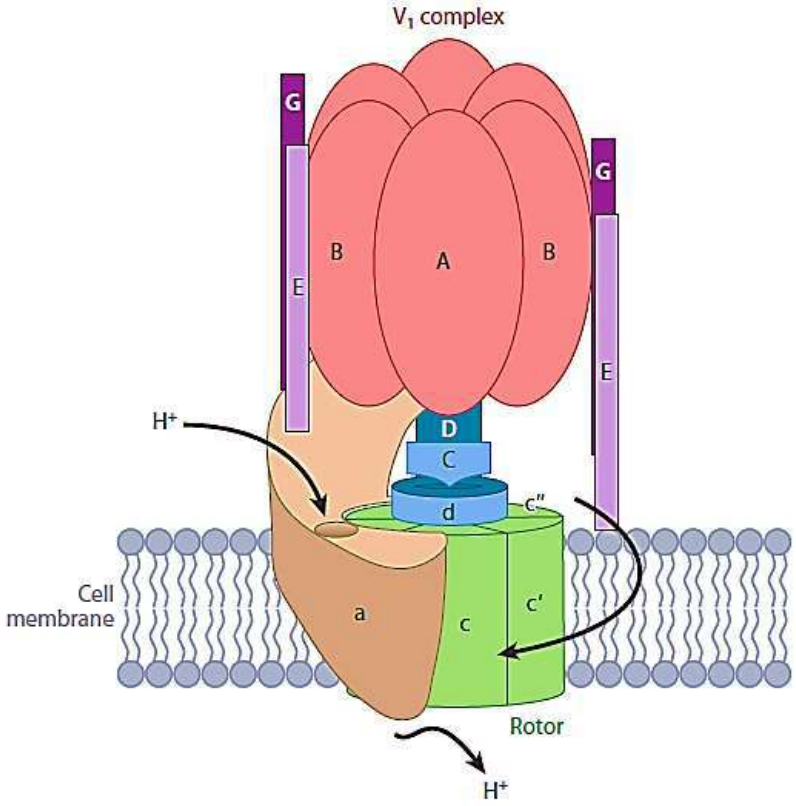
Proton transport inside the lysosome





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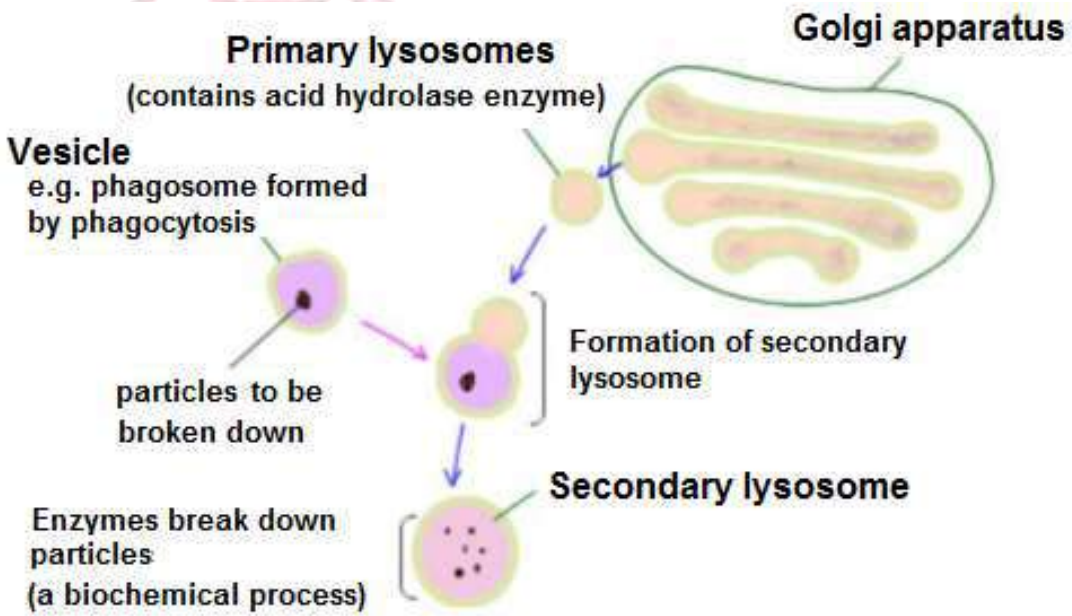
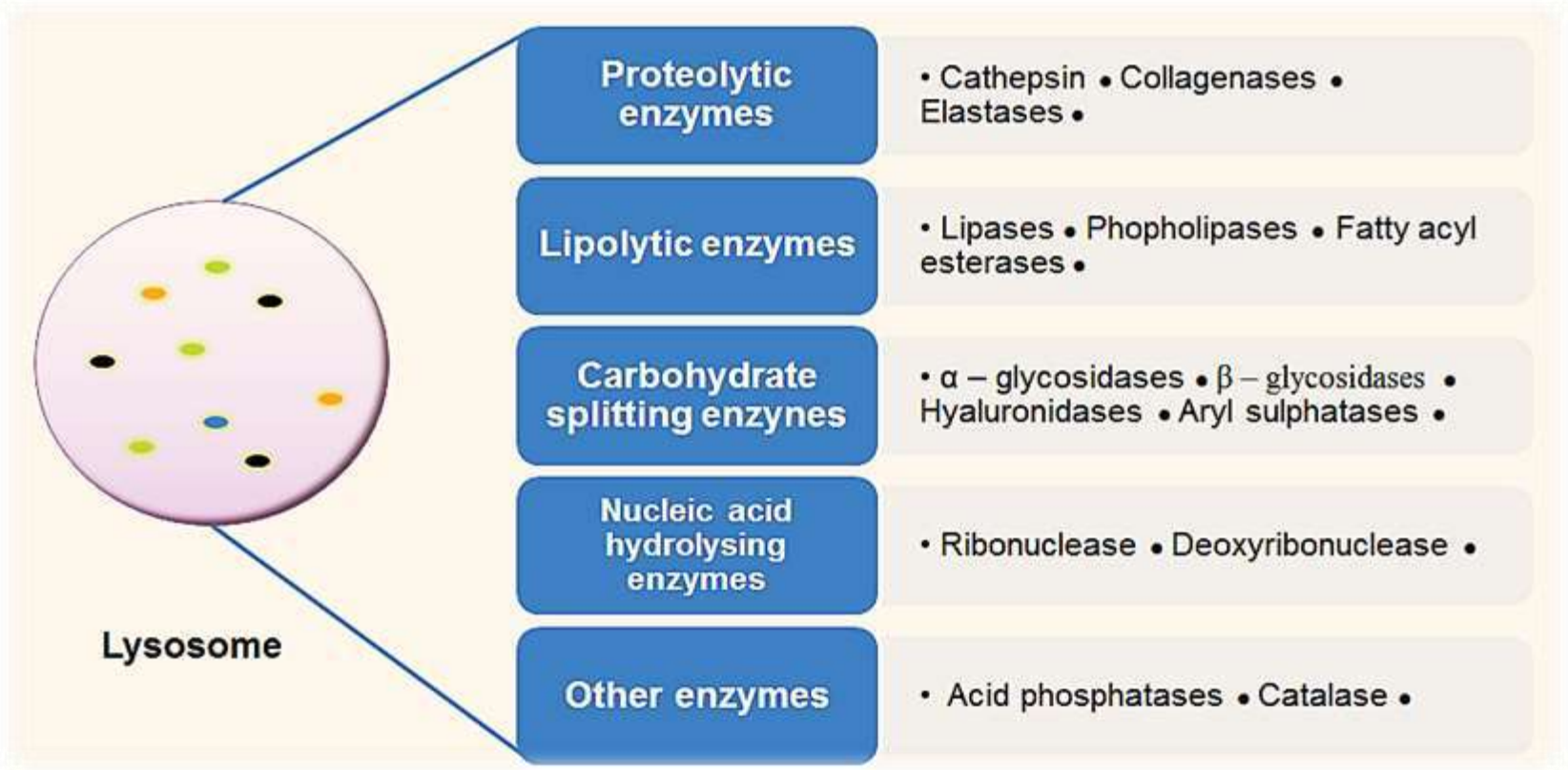
Formation of lysosomes

- Lysosomes are formed by the fusion of transport vesicles budded from the trans-Golgi network with endosomes, which contain molecules taken up endocytosis at the plasma membrane.
- The hydrolytic enzymes formed in rough RER are tagged with mannose-6-phophate by the enzymes *N-acetylglucosamine phosphotransferase* and *N-acetylglucosamine phosphoglycosidase* within the Golgi apparatus to target them to the lysosome.

- The tagged enzymes buds off from the Golgi and the nascent vesicles then bind to a late endosome which is another acidic, membrane-bound organelle.
- The late endosome has proton pumps within its membrane that keep its internal environment acidic.



Proton transport and activation of enzyme



- These enzymes are present in inactive state (zymogen) in the lysosome.
- The enzymes are activated upon increase in acidity of lysosome upon proton influx.

Functions of lysosomes

Lysosomes serve two major functions;.

- Intracellular digestion
  - Primary lysosome fuses with the membrane of food vacuole and squirts the enzymes to food vacuole side.
  - Digested food then diffuses through the vacuole into the cytosol to be used for energy and growth.

- Autolytic action
  - Cell organelles that are no longer needed are engulfed by the lysosome to form *autophagosome*.
  - Cell organelles inside the autophagosome are then degraded by the hydrolytic enzymes of lysosomes.
  - Simple molecules after digestion diffuse to the cytosol to be used for energy and growth.

Functions of lysosomes

Processes in which lysosomes are involved

- Heterophagy is the taking up of exogenous particles by the process of phagocytosis or pinocytosis to form phagosome, which later fuses to primary lysosome to form heterophagosome. Nutirents obtained after digestion of Ingested particles in heterophagosome are released into the cytosol.

- Autophagy is the process in which subcellular organelles are taken up the lysosomal vesicles and degraded by the hydrolytic enzymes contained in the lysosomes. This process leads to the destruction of cells in the body also termed as cell suicide.

- Extracellular digestion where a cell secretes hydrolases outside by exocytosis resulting in the degradation of extracellular matrix, e.g., cells of the digestion lining alimentary canal, secretion by saprophytic enzymes, etc.

Functions of lysosomes

Processes in which lysosomes are involved

- Autolysis is the process where the killing of an entire set of cells occurs by the breakdown of the lysosomal membrane. The autolysis occurs mainly during metamorphosis of amphibians and insects.

- Fertilization involves the rupture of acrosomal membrane which results in the release of enzymes on the surface of the egg. Acrosomes are basically a modified form of lysosome can be termed a giant lysosome forming sperm head. The rupture of sperm/ acrosomal head paves the way for the entry of sperm into the egg by digesting the egg membrane.

Maintaining of acidic pH is necessary for the effective functioning of lysosomes

Clinical relevance

Lysosomal function has also clinical relevance. Malfunctioning of lysosomes may lead to different pathophysiological conditions. These are as follows:

- I-cell disease
  - It is an autosomal recessive disorder.
  - It is caused by genetic defects due to mutation of N-acetylglucosamine phosphotransferase enzyme.
  - It leads the lysosomal enzymes not being properly targeted.
  - As a result significant amounts are found in both the urine and the blood.
  - It results in the accumulation of debris within the cells that forms the characteristic intracellular inclusions, hence the name of the disease causes mucolipidosis.
  - Characteristic feature of this disease is the presence of lipids, glycosaminoglycans (GAGs) and the carbohydrates in the blood (differentiates from Hurler syndrome).

- Lysosomal storage disease
  - The most common pathophysiological condition of this type disease is the Gaucher's disease.
  - It is caused by the a deficiency of the beta-glucocerebrosidase which is responsible for breakage of glucocerebroside. Deficiency leads to its accumulation in the cells.
  - Symptoms include hepatosplenomegaly and anaemia.

Further readings

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